

U.S. SERIAL NO: 08/126,505
FILED: September 24, 1993
AMENDMENT

repeats derived from a second, different complement regulating protein, complement regulating protein analogs wherein the short consensus repeats are rearranged, and complement regulating protein analogs consisting of as few as three short consensus repeats, wherein the protein analog binds C3b, C4b or C3b and C4b.

8. (four times amended) An analog of a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and [those] these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains [a change within a] amino acid substitutions in the short consensus [repeat that corresponds] repeats which correspond [with a change to] to amino acid substitutions in the short consensus repeats of complement receptor one [as shown in Sequence] (SEQ ID No[.]: 13) selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) (Sequence ID Nos 1 and 3) replaced with CR1 amino acids 497-618 (SCR 8-9) (Sequence ID Nos. 2 and 4) and CR1-4(8,9) with deletion of 194-253; and substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-

E-P-H-V-K (Sequence ID No. 11), or structurally similar amino acids.

9. (five times amended) An analog of a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and [those] these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains [a change within a] amino acid substitutions in the short consensus [repeat that corresponds] repeats which correspond [with a change to] to amino acid substitutions in the short consensus repeats of complement receptor one [as shown in Sequence] (SEQ ID No[.]: 13) selected from the group consisting of:

79: D (amino acid 19 of Sequence ID No. 4); 37,79: Y,D (amino acid 37 of Sequence ID No. 2 and amino acid 19 of Sequence ID No. 4); 92: T (amino acid 32 of Sequence ID No. 4); [109-112: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q (amino acids 49-52, 54-57, 61 of Sequence ID No. 4); 114-117, 121: S-T-K-P...Q; (amino acids 54-61 of Sequence ID No. 4) 116: K (amino acid 56 of Sequence ID No. 4); 116,117: K-P (amino acids 56-57 of Sequence ID No. 4);] 92-94: K...Y (amino acids 32-34 of Sequence ID NO. 3); 99,103,106: S...T...I

U.S. SERIAL NO: 08/126,505
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(amino acids 39, 43 and 46 of Sequence ID No. 3); 109-112: D-T-V-I (amino acids 49-52 of Sequence ID No. 3); 110: T (amino acid 50 of Sequence ID No. 3); 111: V (amino acid 51 of Sequence ID No. 3); 112: I (amino acid 52 of Sequence ID No. 3); [114: D (amino acid 54 of Sequence ID No. 3); 115: N (amino acid 55 of Sequence ID No. 3); 121: D (amino acid 61 of Sequence ID No. 3); 117: T (amino acid 57 of Sequence ID No. 3);] 1,3: Q...N (amino acids 1, 3 of Sequence ID No. 1); 6-9: E-W-L-P (amino acids 6-9 of Sequence ID No. 1); 12-16, 18-21: K-L-K-T-Q...N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 27,29: S...K (amino acids 27,29 of Sequence ID No. 2); 37: S (amino acid 37 of Sequence ID No. 1); 44, 47, 49: I...K...S (amino acids 44, 47, 49 of Sequence ID No. 1); 52-54, 57, 59: T-G-A...R...R (amino acids 52-54, 57, 59 of Sequence ID No. 1); 78-79, 82: K-G...F (amino acids 18-19, 22 of Sequence ID No. 3); 85, 87: Q...K (amino acids 25, 27 of Sequence ID No. 3); 12-16, 18-21: R-P-T-N-L...D-E-F-E (amino acids 12-21 of Sequence ID No. 1); 27,29: Y...N (amino acids 27, 29 of Sequence ID No. 1); 35, 64-65, 94: G...R-N...Y (amino acid 35 of Sequence ID No. 1, amino acids 4-5, 34 of Sequence ID No. 3), substitutions with structurally similar amino acids, and combinations thereof.

16. (three times amended) A method for making an analog of a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the

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group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, comprising

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constructing a DNA sequence encoding a protein analog selected from the group consisting of complement regulating protein analogs containing short consensus repeats derived from a second, different complement regulating protein, complement regulating protein analogs wherein the short consensus repeats are rearranged, and complement regulating protein analogs consisting of as few as three short consensus repeats, wherein the protein analog binds C3b, C4b, or C3b and C4b, and

expressing the DNA sequence in a suitable host for expression of the protein.

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23. (four times amended) A method for making a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and [those] these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains [a change within a] amino acid substitutions in the short consensus

U.S. SERIAL NO: 08/126,505
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[repeat that corresponds] repeats which correspond [with a change to] to amino acid substitutions in the short consensus repeats of complement receptor one [as shown in Sequence] (SEQ ID No[.]: 13) selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) (Sequence ID Nos. 1 and 3) replaced with CR1 amino acids 497-618 (SCR 8-9) (Sequence ID Nos. 2 and 4) and CR1-4(8,9) with deletion of 194-253; substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K (Sequence ID No. 11), or structurally similar amino acids.

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cont.
24. (four times amended) A method for making a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and [those] these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains [a change within a] amino acid substitutions in the short consensus [repeat that corresponds] repeats which correspond [with a change to] to amino acid substitutions in the short consensus repeats of complement receptor one [as shown in Sequence] (SEQ ID No[.]: 13) selected from the group consisting of:

U.S. SERIAL NO: 08/126,505
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79: D (amino acid 19 of Sequence ID No. 4); 37,79: Y,D (amino acid 37 of Sequence ID No. 2 and amino acid 19 of Sequence ID No. 4); 92: T (amino acid 32 of Sequence ID No. 4); [109-112: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q (amino acids 49-52, 54-57, 61 of Sequence ID No. 4); 114-117, 121: S-T-K-P...Q; (amino acids 54-61 of Sequence ID No. 4) 116: K (amino acid 56 of Sequence ID No. 4); 116,117: K-P (amino acids 56-57 of Sequence ID No. 4);] 92-94: K...Y (amino acids 32-34 of Sequence ID NO. 3); 99,103,106: S...T...I (amino acids 39, 43 and 46 of Sequence ID No. 3); 109-112: D-T-V-I (amino acids 49-52 of Sequence ID No. 3); 110: T (amino acid 50 of Sequence ID No. 3); 111: V (amino acid 51 of Sequence ID No. 3); 112: I (amino acid 52 of Sequence ID No. 3); [114: D (amino acid 54 of Sequence ID No. 3); 115: N (amino acid 55 of Sequence ID No. 3); 121: D (amino acid 61 of Sequence ID No. 3); 117: T (amino acid 57 of Sequence ID No. 3);] 1,3: Q...N (amino acids 1, 3 of Sequence ID No. 1); 6-9: E-W-L-P (amino acids 6-9 of Sequence ID No. 1); 12-16, 18-21: K-L-K-T-Q...N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 27,29: S...K (amino acids 27,29 of Sequence ID No. 2); 37: S (amino acid 37 of Sequence ID No. 1); 44, 47, 49: I...K...S (amino acids 44, 47, 49 of Sequence ID No. 1); 52-54, 57, 59: T-G-A...R...R (amino acids 52-54, 57, 59 of Sequence ID No. 1); 78-79, 82: K-G...F (amino acids 18-19, 22 of Sequence ID No. 3); 85, 87: Q...K (amino acids 25, 27 of